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Open Access Review Article

Contact Lenses: A Promising Drug Delivery System

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ABSTRACT

Presently, around 100 million people are estimated to be wearing contact lenses, and the number is growing exponentially. Though the main use of contact lenses is for improving ametropia problems, they also hold attention as therapeutic devices for the treatment of ocular pain, promotion of corneal healing, maintenance of corneal epithelial hydration, and drug delivery. Contact lenses are developing as an substitute ophthalmic drug delivery system to resolve the problems of the conventional topical application methods. The interest in evolving contact lenses for drug delivery has expressively increased in the last decade as several new techniques have been developed for designing contact lenses for extended drug delivery. The newest studies show that contact lenses are able to achieve prolonged release of a few weeks without any significant effect on critical lens properties. The future appears promising for drug eluting contact lenses but several challenges remain to be overcome regarding processing and storage issues, lack of use in the elderly population, regulatory issues, high costs of clinical studies and cost-benefit analysis. Contact lenses are attractive for ocular drug delivery systems as significantly prolong the residence time of the drug in the eye, high degree of comfort which improve patient compliance, higher efficiency and low side effects and, hence increase the ocular drug bioavailability.

Keywords: Lenses, polymer, methods, therapeutic, eye

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INTRODUCTION:

Most ophthalmic drugs are applied topically in the form of eyedrops. Adequate therapy from eyedrops is achieved either by providing a sufftcient magnitude of the pulse, so that its effect extends for a useful period of time, or by giving more frequent applications of a less concentrated pulse[1-4]. Ocular drug delivery is troubled by the barriers shielding the eye. The bioavailability of the active drug substance is often the main barrier to overcome. Conventional ocular dosage form, including eye drops, is no longer sufficient to fight against ocular diseases. Apart from this contact lenses have been widely used to correct vision by directly placing them on the outer surface of the eyes. Beginning recently, contact lenses have also been used for therapeutic purposes. Ocular drug delivery to the eyes through contact lenses has received much attention order to achieve an effective drug delivery system using contact lenses, several technical issues, such as short drug release time and limited drug loading, should be addressed. Researchers explored various strategies including vitamin loading, molecular imprinting, and nanoparticle embedding, to overcome the hurdles[6] . Several eye diseases like cataract, age-related macular degeneration, diabetic retinopathy, glaucoma etc have reported to affect several millions of the world population. The intraocular and systemic therapy is not widely used due to their intrinsic limitations. The topical route is the most appropriate therapy for local and controlled delivery of bioactive and therapeutic molecules to the eye, as it offers higher patient compliance, better proximity to the infected site and a have less potential systemic side effects. Among the topical formulations, conventional topical eye drops is well recognized. However, the achievement of topical therapy is limited by some issues such as low bioavailability (>1%), short residence time, low corneal permeability. Therefore products such as contact lenses, have been launched in the market while many others are in pre-clinical and clinical stages[7]. Contact lenses

includes polymeric/ mucoadhesive formulations, hydrogels, in situ gelling systems etc. Contact lenses are particularly attractive for ODDS as these significantly increase the residence time (typically days) of the drug in the eye, high degree of comfort and enhances the drug bioavailability considerably [8] . Contact lenses for ophthalmic drug delivery widespread, due to their advantages like extended wear and more than 50% bioavailability. To attain controlled and sustained drug delivery from contact lenses, researchers are working on various systems like polymeric nanoparticles, microemulsion, micelle, liposomes, use of vitamin E, etc. Many scientists are working on different areas of therapeutic contact lenses to treat ocular diseases by developing techniques like soaking method, molecular imprinting, entrapment of drug colloidal nanoparticles, drug plate/film, ion ligand polymeric systems, supercritical fluid technology, etc [9].

METHODOLOGY TO DESIGN THERAPEUTIC CONTACT LENSES:

1. Soaking method

It is the most simple, cost effective and conventional way to load drug into the contact lenses. This method involves soaking the preformed contact lenses in the drug solution, followed by drug uptake and release in pre- and post-lens tear film. The contact lenses are available as solid or may have the cavity for receiving the drug solution. Their drug reservoir ability strongly depends on the water content, thickness of lenses, the molecular weight of the drug, soaking time period and concentration of drug in soaking solution. As an alternative, one can also insert contact lenses into the eyes and then apply eye drops. By this means, drugs can be absorbed and released by the contact lens. Use of therapeutic contact lenses prepared by soaking method, to deliver ophthalmic drugs like timolol, pilocarpine, dexamethasone, hyaluronic acid, brimonidine tartrate etc. have been explored by many researchers[9,10].

2. Molecular imprinting

The utilization of the molecular imprinting technique is an important progress in this line of work. The spatial arrangement of monomers becomes permanent when the polymerization process is completed. Molecular imprinting (MI) is one of the advanced methodologies using hydrogel contact lenses for high drug loading and controlled drug delivery. The procedure consists in synthesizing the contact lens in the presence of the drug molecules which act as a mold causing monomers to arrange themselves according to their affinity. The procedure consists in synthesizing the contact lens in the presence of the drug molecules which act as a mold causing monomers to arrange themselves according to their affinity. The monomers in the hydrogel matrix are prepared in such a way that high drug affinity molecular sites are created. These molecular imprinted sites mimic the drug's receptors, which increase drug loading capacity[9,13].

Types of hydrogels:

1. Poly-2-hydroxyethylmethacrylate (pHEMA) hydrogels.

2. HPMA copolymer

3. Acrylamide (AAm) hydrogel

4. Silicon hydrogel

4. NHS–PEG–biotin hydrogel[10].

3. Colloidal nanoparticles loaded therapeutic contact lens

The technique is based on the ability of colloidal nanoparticles (polymeric nanoparticles, liposomes, niosomes, microemulsion, micelles, etc.) to entrap or encapsulate drug and control its release rate from contact lenses. Such formulated nanoparticular system (10 to 100 nm) is dispersed in HEMA monomers and polymerized using ethylene glycol-dimethacrylate (EGDMA) and photo initiator (Darocur_) to fabricate therapeutic contact. Drug laden nanoparticles prevent the interaction of drug with polymerization mixture and also offer additional resistance to drug release. Thus the nanoparticles loaded contact lenses can deliver drugs at controlled rate for extended period of time. Drug loaded nanoparticles or globules (microemulsion) also bypass, to some extent, drug metabolism from the enzymes like lysosomes, present in the tear/corneal epithelial surface. This technique is successful in developing therapeutic contact lenses for extended drug delivery, while at the same time the transparency (optical), oxygen permeability, ion permeability, mechanical properties, and swelling behavior of contact lenses was altered for comfort wear[9].

4. Polymeric nanoparticles

Many researchers have done their research upon polymeric nanoparticles using biodegradable and non-biodegradable polymers, to formulate therapeutic contact lenses to treat ocular diseases. These polymeric nanoparticles are developed to treat glaucoma, by dispersing timolol loaded propoxylated glyceryl triacylate (PGT) nanoparticles in contact lenses. This system showed sustained release, the incorporation of nanoparticle in the silicone hydrogel contact lenses caused reduction in both ion and oxygen permeability, and an increase in storage modulus, suggesting the limitation of the technique [9,12].

Table 1: Characteristics of various polymers as vehicle for therapeutic contact lenses[10,12]

Sr. No.	Polymer	Characteristics
1.	Propoxylated glyceryl triacrylate (PGT)	Polymer having multiple vinyl functionalities
2.	Polycaprolactone (PCL)	Hydrophobic and FDA-approved bioresorbable polymer without toxic byproducts
3.	Chitosan	Cationic polysaccharide polymer with good biocompatibility and biodegradability including lysozyme-related degradability
4.	poly-(lactic-co-glycolic acid) (PLGA)	Biocompatible, biodegradable and FDA-approved polymer that can change properties by varying the ratio of glycolic acid to lactic acid
5.	Poly (D,L-lactide)-dextran (Dex-b-PLA)	Core-shell structured nanoparticles containing PLA core and dextran outer shell

5. Cyclodextrins

In another approach, polymers like cyclodextrins (CDs) and their derivatives were used to achieve sustained drug delivery of hydrophobic drugs. CDs can accommodate many different hydrophobic molecules in their hydrophobic interior (ringshaped structure), to achieve controlled drug delivery. The incorporation of b-CD in the hydrogels resulted in increased swelling and tensile strength. The cyclodextrins loaded contact lenses are effective to treat glaucoma. Invitro studies, reported an increase in the drug solubility in poly-CD, an increase of its concentration in the cornea and an extended release over several weeks.

6. Liposomes

Liposomes are biocompatible and biodegradable, due to their biological membrane-like structure and used in numerous drug delivery applications including ophthalmic drug delivery through contact lenses. Multilamellar lipososmes showed greater sustained release in comparison to REL liposomes, because of the presence of several lipid bilayers[9].

7. Microemulsion and micelles

Drug-loaded microemulsion and micelles loaded therapeutic contact lenses showed promising results, due to their thermodynamic stability, easy preparation, high drug-loading capacity, increased wettability (low protein adherence) and easy tailoring of drug release pattern. Due to nano size (5100 nm) the optical property of hydrogels remained unaltered eg. timolol-contact lenses with o/w type. The microemulsion showed controlled release of timolol, due to the presence of a tightly packed surfactant at the oil–water interface. This system involves use of surfactant. The presence of surfactant did not alter the optical property of the contact lenses, and also had the advantage of increase in wettability, i.e. reduction in protein absorption on contact lens surface[9].

8. Use of vitamin E

To improve the drug-release duration Vitamin E is used as transport barriers for drug molecules. The release of timolol was significantly extended by increasing Vitamin E loading from 10 to 40% in contact lenses, while at the same time complicating oxygen and ion permeability[9].

9. Supercritical fluid technology

Supercritical fluid technology (SCF) is one of the most effective technologies to load/impregnate both hydrophilic and hydrophobic drug in contact lenses using supercritical solvent like CO2. Impregnation process involve dissolution of drug in supercritical solvent like CO2 (at subcritical or supercritical conditions), followed by interaction with hydrogel contact lenses. The drug loading amount and its release kinetics are controlled by tailoring operational parameters like pressure, temperature, processing time and depressurization rate[9].

CHARACTERISTICS OF MEDICATED CONTACT LENSES

(1) Transparency Of The Lens:

(2) Oxygen Permeability:

(3) Glass Transition Temperature:

(4) Wettability:

(5) Water Content:

(6) Drug Loading In Preformed Lenses:

1) Transparency of the lens:

Optical clarity is important during developing contact lens and it should be maintained after incorporation of drugs. Novel approaches have enabled to generate contact lens drug delivery systems with acceptable transparency, although it could be improved in some cases. For instance, contact lenses formulated with advanced techniques such as molecular imprinting and supercritical solvent approaches, loaded liposomes and microemulsions, exhibited good transparency[1,8].

2) Oxygen permeability:

Drug eluting contact lens should allow transfer of oxygen to the eyes since low oxygen permeability can cause severe side effects, such as corneal edema. Hence, the prepared lenses should allow free transfer of oxygen to the eyes and any low oxygen transfer eventually causes severe side effects. To avoid hypoxia, a minimum value of oxygen transmissibility (Dk/t) around 125 has been suggested.

Eg. The silicone hydrogel contact lens, also known as siloxane lens, show impressive permeability while retaining the comfort, wettability and biofilm resistance of non-silicon based hydrogels[1,8].

3) Glass transition temperature:

The Tg (Glass transition temperature) of contact lenses is not expected to alter during the drug loading process or due to incorporation of additives. Glass transition temperature has been measured in drug eluting contact lenses manufactured by various approaches. Several studies indicate that the contact lenses manufactured by various approaches have not shown any significant effect on Tg. Further, the alteration in Tg on addition of βCD was found to be insignificant, which suggests that the grafted βCD has little or no effect on the degree of cross-linking of the hydrogels or the stiffness of the network[1,8].

4) Wettability:

Wettability of contact lenses is a critical variable that affects their physiological compatibility and the stability of the prelens lacrimal fluid. It can be determined by contact angle measurements. Hydrophobic polymers will repel the water that makes up a majority of the tear surface. This disrupts the tear flow and results in the deposition of an albumin film on the lens, which eventually reduces the effectiveness of the contact and can cause infection and/or irritation. Therefore, if a contact lens surface is highly hydrophobic it needs to be made hydrophilic. Doping the polymer or treating the surface of the polymer can do this change in the morphology of the surface[1,8].

5) Water content

Water content of contact lenses is crucial as it likely impacts comfort and an increase in the water content enhances the oxygen permeability of contact lenses. The permeability of the lens is proportional to the amount of water in the lens. As the percent weight of water increases in the lens, the permeability increases linearly. The ability of lenses to absorb large amounts of water also makes them highly hydrophilic. These attributes gives soft contact lenses the ability to achieve greater permeability and could be used for extended wear without disturbing the eye. However, achieving greater permeability is a complex issue as increase in water content will eventually loose the polymer strength. This can lead to tearing or scratching of the lens[1,8].

CONTACT LENSES FOR OCULAR DRUG DELIVERY

1. Allergic conjunctivitis

Allergic conjunctivitis affects up to 40% of the general population, with seasonal allergic conjunctivitis accounting for up to 90% of these ocular cases. Antihistamines, such as ketotifen fumarate, are used to alleviate the sign and symptoms of allergic conjunctivitis through multiple pharmacological actions. In in vitro assays, all the contact lenses released an amount of ketotifen fumarate higher than the dosage provided by eye drops with the majority of the drug released within the first hour[1,15].

2. Dry eye

The dry eye syndrome is a multifactorial disease of the tears and the ocular surface, associated with discomfort symptoms, visual disturbance, and tear film instability. In severe cases, this may lead to ocular surface damage. Common clinical signs of a patient with dry eye syndrome include inflammation, increased osmolarity, decreased tear breakup time, and ocular surface epithelial damage. Various molecules working as rewetting agents, such as hyaluronic acid or hydroxypropyl methylcellulose, have been also included in SCLs and their subsequent release have been analyzed. This lens combination device can provide great comfort in dry eyes and it can be particularly valuable for combating contact lens-induced dry eye[1,15].

3. Glaucoma

Glaucoma is a group of progressive optic neuropathies, characterized by the damage caused to the optic nerve, fiber layer, and ganglion cells. If it is not treated, it results in visual field loss.An important risk factor for the nerve damage is the elevated intraocular pressure (IOP), and the restoration of the IOP to the normal level is the most common treatment for glaucoma. Several different classes of drugs are currently prescribed with this purpose, such as prostaglandin analogs, beta-adrenergic receptor antagonists, carbonic anhydrase inhibitors, and alpha2-adrenergic agonists Patients wearing the contact lenses for 30 min per day for 2 weeks showed IOP values equivalent to those obtained with previous eye drop treatment and no ocular toxicity was observed[1,15,16].

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